



Screening adult tuberculosis patients for diabetes mellitus in Ebeye, Republic of the Marshall Islands

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A retrospective cohort study was conducted to evaluate the screening of adult TB patients for diabetes (DM) using glycated haemoglobin (HbA_{1c}) in Ebeye, Republic of the Marshall Islands. Of 62 patients registered between July 2010 and December 2012, 28 (45%) had DM. The only significant difference in baseline characteristics between those with and those without DM was higher age in those with DM. Two-month sputum smears and cultures were also not different between the two groups. Despite the limited sample size, this study shows that screening TB patients for DM in Ebeye is feasible and worthwhile and that it should be continued.

Recent evidence confirms a significant link between diabetes mellitus (DM) and tuberculosis (TB).^{1,2} The interaction between these two diseases is apparent, and National Tuberculosis Programmes (NTPs) in many Pacific Island TB clinics have anecdotally reported a high prevalence of DM in patients registered and treated for TB. DM not only increases the risk of TB, it may also complicate anti-tuberculosis treatment, with possible delays in sputum culture conversion, increased risk of death and increased risk of recurrent disease after successful completion of treatment.^{3,4}

Ebeye Island, a small 0.4 km² atoll in the Republic of the Marshall Islands (RMI), has a single 45-bed hospital and three dispensary health centres, staffed by health assistants. RMI has a high prevalence of DM type 2, with nearly 20% of the adult population affected.⁵ TB incidence rates are also relatively high, with a reported incidence of 222 per 100 000 population in 2009.⁶ Due to high rates of TB and DM, the RMI NTP initiated screening for DM among all adult TB patients in 2010.

The aim of the present study was to assess baseline demographic and clinical characteristics, 2-month sputum smear and culture results and treatment outcomes of TB patients disaggregated by DM status in Ebeye over a 30-month period from 2010 to 2012.

ASPECT OF INTEREST

This was a retrospective cohort study. Despite its small size and remote location, Ebeye Island is one of the most crowded places on earth, with over 25 000 persons/km².⁵ Ebeye's high population density is due to the immigration of islanders seeking employment at the nearby US Army missile testing site. Poor economic conditions and limited arable land have caused dependence on low-cost imported canned goods as the main food source, leading to an ever-growing bur-

den of non-communicable diseases. A typical household provides shelter for several families,⁵ which may contribute to high rates of TB transmission.

The NTP registers on average 40 patients per year and provides treatment with standard four-drug treatment under directly observed supervision, using World Health Organization (WHO) approved fixed-dose combination tablets.⁷ Recent increases in TB cases, including four multidrug-resistant (MDR-TB) patients in the community, have caused concern within the NTP. In 2010, RMI endorsed the US-Affiliated Pacific Islands Standards for Management of Tuberculosis and Diabetes.⁸ These guidelines, which are line with the recently developed WHO-Union (International Union Against Tuberculosis and Lung Disease) Collaborative Framework for the Care and Control of Tuberculosis and Diabetes, call for routine bidirectional screening of the two diseases and improvement of blood glucose control throughout anti-tuberculosis treatment.⁸

The patient sample included all adult TB patients consecutively registered in the Ebeye NTP from 1 July 2010 to 31 December 2012. Patients were referred from in-patient and out-patient care as well as from TB and DM public health clinics. Data variables collected from TB registers and treatment cards included type and category of TB, baseline chest radiographs (classified as normal, abnormal no cavities or abnormal cavities), sputum smear and culture at baseline and at 2 months, and final treatment outcomes. TB cases were screened for DM using glycated haemoglobin (HbA_{1c}), with a value of ≥ 7.0 used to diagnose DM.

Anonymous data were single-entered into EpiData Version 7.1 (Epidata Association, Odense, Denmark), which was used to analyse and compare characteristics and outcomes by group using relative risk and the χ^2 test. Confidence intervals and levels of significance were set at 5%.

The study protocol was approved by the RMI Assistant Secretary of Health and the Ethics Advisory Group of The Union, Paris, France. Ethics approval was also obtained from the US Centers for Disease Control and Prevention, Atlanta, GA, USA.

Of the 62 consecutive adult TB cases, 28 (45%) were diagnosed with DM. Sociodemographic characteristics and baseline clinical features are shown in Table 1. The main difference was that patients with DM were older than those without. There were no other significant differences between the groups, although a higher proportion of patients with DM had previously undergone treatment for TB and were sputum

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TABLE 1 Demographic and radiographic findings of adult tuberculosis patients with diabetes mellitus, Ebeye, Republic of Marshall Islands, July 2010–December 2012 (*n* = 62)

Characteristic	Diabetics <i>n</i> (%)	Non-diabetics <i>n</i> (%)	RR (95%CI)	<i>P</i> value
Total (<i>n</i> = 62)	28 (45)	34 (55)		
Age, years, mean (95%CI)	53.8 (49.9–57.7)	32.7 (28.8–36.6)		
Sex				0.434
Male	19 (68)	19 (56)	1.25 (0.80–1.95)	
Female	9 (32)	15 (44)		
Ethnicity				
Marshallese	28 (100)	34 (100)		
Non-Marshallese	0 (0)	0 (0)		
TB site				0.366
Extra-pulmonary	1 (4)	4 (12)	0.30 (0.03–2.56)	
Pulmonary	27 (96)	30 (88)		
TB type*				0.200
Relapse	7 (25)	4 (12)	2.12 (0.69–6.52)	
New case	21 (75)	30 (88)		
X-ray category				0.584
Cavitary	7 (25)	11 (32)	0.77 (0.35–1.73)	
Non-cavitary	21 (75)	23 (68)		
Initial smear result*				0.431
Smear-positive	13 (54)	15 (41)	1.33 (0.78–2.28)	
Smear-negative	11 (46)	22 (59)		
Initial culture result†				0.606
Culture-positive	13 (48)	18 (56)	0.86 (0.52–1.40)	
Culture-negative	14 (52)	14 (44)		

*Excludes one patient, as smear was not performed.

†Excludes three cases whose initial culture results were not recorded.

RR = relative risk; CI = confidence interval; TB = tuberculosis.

TABLE 2 Two-month culture result and treatment outcome of adult tuberculosis patients with diabetes mellitus, Ebeye, Republic of Marshall Islands, July 2010–December 2012 (*n* = 56)

Category	Diabetics <i>n</i> (%)	Non-diabetics <i>n</i> (%)	χ^2	RR (95%CI)	<i>P</i> value
Two-month culture result*					
Culture-positive	1 (7)	0 (0)	1.18		0.28
Culture-negative	13 (93)	16 (100)			
Treatment outcome					
Died	5 (19)	2 (7)	2.88 (0.61–13.64)		0.23
Completed	21 (81)	28 (93)			

*Excludes 32 patients with 2-month sample not collected or not recorded.

RR = relative risk; CI = confidence interval.

smear-positive. Two-month culture conversion and final treatment outcomes are shown in Table 2. There were no significant differences between patients with and without DM, although a higher proportion of DM patients died during anti-tuberculosis treatment.

DISCUSSION

This is the first study to evaluate the screening of adult TB patients for DM in RMI and assess associations between the two diseases with respect to baseline characteristics and treatment outcomes. Of importance, all TB patients were screened for DM and nearly half were found to have DM. Patients with DM and TB were older than those who did not have DM, but no other significant differences were found between the two groups.

This study has several strengths: all adult TB patients were included; screening was performed using HbA_{1c}, which shows less variation over time than fasting blood glucose;⁹ and data were collected and recorded in a standardised format. Furthermore, the study adhered to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies.¹⁰ The main limitation was the small sample size, which may have precluded finding other significant associations between groups. Some Ebeye TB cases may also have been diagnosed in nearby Majuro or Hawaii and therefore not recorded, and over half of the 2-month sputum culture results were not available. Procedures for the performance and follow-up of sputum and culture results during treatment thus need to be strengthened.

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Despite the small numbers of patients, this study has important implications for policy and practice. First, it shows that bi-directional screening is feasible, resulting in 100% of adult TB patients being screened for DM. Second, comparisons between the two groups indicate that patients with DM and TB have worse intermediate and final treatment outcomes; this might be amenable to improvement with better management and control of DM. In the Pacific, universal DM screening among adult TB patients is one way of addressing this important challenge.

In conclusion, the Ebeye NTP will continue DM screening to optimise TB-DM patient care, and will continue to collect and report baseline and outcome data from TB-DM patients to provide sound evidence for best practices for other recently integrated programmes in the Pacific Region.

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Une étude rétrospective de cohorte a été réalisée afin d'évaluer le dépistage du diabète (DM) chez des patients tuberculeux adultes grâce à l'hémoglobine glycosylée (HbA_{1c}) à Ebeye, République des îles Marshall. Entre juillet 2010 et décembre 2012, 62 patients ont été enregistrés, parmi lesquels 28 (45%) avaient un DM. La seule

différence significative dans les caractéristiques de départ entre les patients était un âge plus avancé pour les diabétiques. Les frottis et cultures de crachats à 2 mois étaient similaires. Malgré la taille limitée de l'échantillon, cette étude montre que le dépistage du DM chez les patients tuberculeux est faisable et utile et devrait être poursuivi.

Se llevó a cabo un estudio retrospectivo de cohortes con el fin de examinar la detección sistemática de la diabetes mellitus (DM) en los pacientes adultos con diagnóstico de tuberculosis (TB), mediante la determinación de la hemoglobina glucosilada (HbA_{1c}) en Ebeye, en la República de las Islas Marshall. Se registraron 62 pacientes entre julio del 2010 y diciembre del 2012, de los cuales 28 eran diabéticos (45%). La única diferencia significativa en las

características iniciales de los pacientes con y sin DM fue una edad mayor de los pacientes con DM. No se observó diferencia entre los grupos de los resultados de la baciloscopia ni el cultivo del esputo a los 2 meses. Pese al tamaño reducido de la muestra, el presente estudio pone en evidencia que la detección sistemática de la DM en los pacientes con diagnóstico de TB es factible, útil y que se debe continuar.